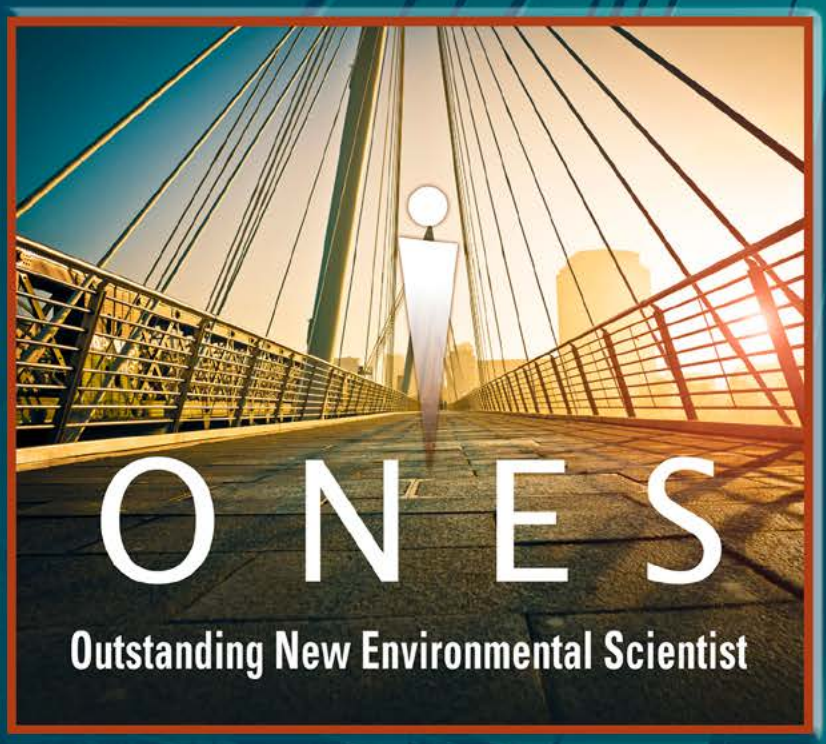
National Institute of Environmental Health Sciences



Awardee Symposium

July 1-2, 2014

Tuesday, July 1, 8:00 a.m. – 4:30 p.m.
NIEHS Building 101, Rodbell BC

Wednesday, July 2, 8:30 a.m. – 2:30 p.m.
NIEHS Building 101, Rodbell BC

National Institutes of Health • U.S. Department of Health and Human Services

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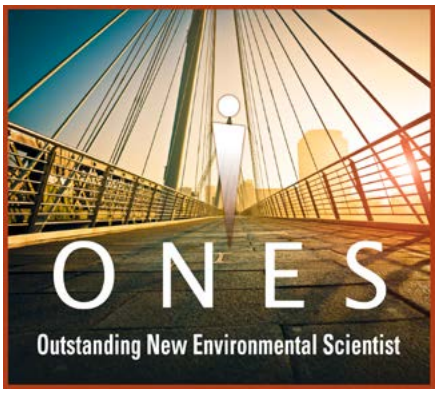

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Awardee Symposium

July 1, 2014 • AGENDA

NIEHS Building 101, Rodbell BC • Research Triangle Park, NC

8:00 a.m.	Linda Birnbaum, *Director, NIEHS*	Welcome
8:15 a.m.	**Michael Humble, *NIEHS, Genes, Environment, and Health Branch (GEHB), Moderator***	**Exposure Biology**
8:20 a.m.	Christina Porucznik, *The University of Utah School of Medicine*	Periconceptional Exposure Assessment – Progress and Preliminary Findings
8:40 a.m.	Lauren Aleksunes, *Rutgers University*	When the Placental Barrier Fails: Mechanisms that Reduce Transporter Function
9:00 a.m.	Vishal Vaidya, *Harvard Medical School*	Modernizing Toxicology: Biomarkers and Cell-Based Approaches to the Rescue
9:20 a.m.	James Luyendyk, *Michigan State University*	Hepatoprotective Effects of Fibrin(ogen)-Integrin Engagement in Liver Injury and Fibrosis
9:40 a.m.	Angela Slitt, *University of Rhode Island*	Going Beyond the Antioxidant Response: Nrƒ2 as a Metabolic Regulator
10:00 a.m.	Break	
10:25 a.m.	**Patrick Mastin, *NIEHS, Deputy Director, Division of Extramural Research and Training (DERT), Moderator***	**Nanotoxicology**
10:30 a.m.	Timothy Nurkiewicz, *West Virginia University School of Medicine*	Nanomaterial Inhalation Exposure and Microvascular Endpoints: Our Journey from an Obscure Skeletal Muscle to the Fetus
11:00 a.m.	Jared Brown, *University of Colorado*	Nanoparticle-Immune Interactions from a Biophysical to Physiological Perspective
11:20 a.m.	Alexander Star, *University of Pittsburgh*	Investigation and Mitigation of Carbon Nanomaterial Toxicity
11:40 a.m.	Stacey Harper, *Oregon State University*	Integrative Studies to Define Drivers of Nanomaterial Toxicity
12:00 p.m.	Lunch	
1:00 p.m.	**Daniel Shaughnessy, *NIEHS, Exposure, Response, and Technology Branch (ERTB), Moderator***	**Environmental Mutagenesis and DNA Repair**
1:05 p.m.	Patricia Opresko, *University of Pittsburgh Graduate School of Public Health*	Mechanisms of Telomere Damage and Repair
1:25 p.m.	Joel Meyer, *Duke University*	Fate and Effects of Persistent Mitochondrial DNA Damage
1:45 p.m.	Jason Bielas, *Fred Hutchinson Cancer Research Center*	Mechanisms of Mitochondrial Mutagenesis
2:05 p.m.	Sarah Delaney, *Brown University*	Inflammation as a Mediator of Dynamic DNA Mutations
2:25 p.m.	Break	
2:50 p.m.	Scott McCulloch, *North Carolina State University*	Preventing Mutations by Making Mutations – Investigating the Molecular Mechanism of Translesion Synthesis by Human DNA pol η.
3:10 p.m.	Yu-Ying He, *The University of Chicago*	Mechanism of UVA-Induced Skin Cancer
3:30 p.m.	Joseph Shaw, *Indiana University*	Effects of Environmental Contamination on Gene Copy Number Variation: Molecular Blueprint for Adaptation, Susceptibility, and Disease
3:50 p.m.	Rebecca Fry, *University of North Carolina-Chapel Hill*	Prenatal Arsenic Exposure, Shifts in Cell Signaling Pathways and Newborn Health Effects
4:10 p.m.	Discussion and Close	
4:30 p.m.	Adjourn	

National Institute of Environmental Health Sciences

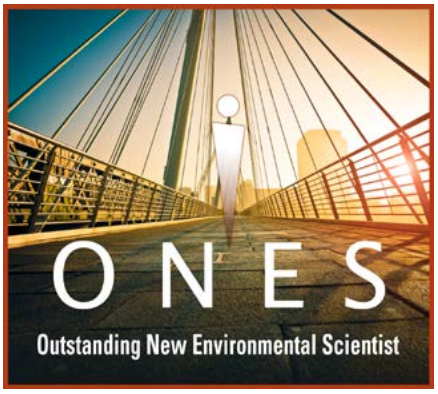
Awardee Symposium

July 2, 2014 • AGENDA

NIEHS Building 101, Rodbell BC • Research Triangle Park, NC

WEDNESDAY, July 2, 2014 – Rodbell BC

Time	Presenter	Presentation Title/Topic
8:30 a.m.	**Janice Allen, *NIEHS, Scientific Review Branch (SRB), Moderator***	**Pulmonary and Cardiovascular Effects**
8:35 a.m.	Gokhan Mutlu, *The University of Chicago*	Role of β_2-adrenergic Receptors in Particulate Matter-Induced Lung Inflammation and Thrombosis
8:55 a.m.	Jill Poole, *University of Nebraska Medical Center*	The Role of Pattern Recognition Receptors in Organic Dust-Induced Airway Inflammation
9:15 a.m.	Brent Carter, *University of Iowa Carver College of Medicine*	Modulation of the Mevalonate Pathway by Akt Controls Macrophage Survival and Development of Pulmonary Fibrosis
9:35 a.m.	**Jonathan Hollander, *NIEHS, Genes, Environment, and Health Branch (GEHB), Moderator***	**Neurotoxic Mechanisms**
9:40 a.m.	Wenbin Deng, *University of California-Davis*	Stem Cells for Neural Regeneration, Drug Discovery, and Toxicology Studies
10:00 a.m.	Break	
10:30 a.m.	Aaron Bowman, *Vanderbilt University*	A Manganese-Handling Deficit in Huntington's Disease Selectively Impairs ATM-p53 Signaling
10:50 a.m.	Jason Richardson *Rutgers Robert Wood Johnson Medical School*	Translational Studies on the Role of Developmental Pyrethroid Exposure in ADHD: Experience with the ViCTER Mechanism
11:10 a.m.	Sven-Eric Jordt, *Duke University School of Medicine*	Sensory TRPA1 Channels Control Inflammation and Pruritogen Responses in Allergic Contact Dermatitis
11:30 a.m.	Lunch	
12:30 p.m.	**Gwen Collman, *NIEHS, Director, Division of Extramural Research and Training (DERT), Moderator***	**Career Insights from ONES and Discussions with NIEHS Program Directors *(and NIEHS postdocs)***
2:30 p.m.	Adjourn	



Presentation Abstracts

Lauren Aleksunes
Rutgers University
"When the Placental Barrier Fails: Mechanisms That Reduce Transporter Function"

The breast cancer resistance protein (BCRP, *ABCG2*) is an efflux transporter expressed in the human placenta that is responsible for the fetal-to-maternal transport of drugs and chemicals. Reduced function of BCRP, as a result from chemical inhibition, genetic polymorphisms or pathology, may be a mechanism involved in the susceptibility of the developing fetus to the toxicity of xenobiotics. The purpose of this presentation is to discuss the interaction of BCRP with environmental chemicals and to highlight genetic, transcriptional, and pathologic mechanisms that regulate BCRP expression and function in the placenta. Understanding how loss of BCRP function affects the placental transfer of xenobiotics will provide insight into potentially susceptible populations at risk of altered developmental programming following *in utero* chemical exposure.

Jason Bielas
Fred Hutchinson Cancer Research Center
"Mechanisms of Mitochondrial Mutagenesis"

Mitochondria are functionally diverse organelles with a central role in many cellular processes, including oxidative phosphorylation and apoptosis. The mitochondrial theory of aging postulates that the lifelong accumulation of mitochondrial DNA (mtDNA) mutations in multiple tissues leads to mitochondrial failure, downstream processes such as apoptosis, and the progressive decline of tissue function (i.e., aging and disease). Moreover, mtDNA mutations are suspected to contribute to the etiology of a number of age-related disorders, including Parkinson's disease, muscle-wasting, and the metastatic potential of cancers. As eukaryotic cells contain many hundreds copies of mtDNA, it stands to reason that a minimum critical number of mutant mtDNAs must be present before tissue dysfunction and clinical signs become apparent. Yet, we do not fully understand the mechanisms underlying the amplification and fixation of these pathogenic mutant populations. There is evidence that these mutations pre-exist at extremely low frequency as random mutations in normal cells and tissues. Our working hypothesis is that the induction and accumulation of random mtDNA mutations fuels pathogenic mutant populations, aging, and age-related disease. Thus, environmental mutagens in particular may play a substantial role in the origin and incidence of aging and disease by damaging mtDNA and increasing the rate at which mitochondrial mutations accumulate. The goal of this proposal is to determine the molecular mechanisms of somatic mtDNA mutagenesis associated with DNA damaging agents and disease, under the direction of the following Aims: (1) test the hypothesis that the frequency of random mtDNA mutations increases with age in humans, (2) determine whether an environmental toxin can increase the rate at which mitochondrial mutations accumulate, (3) evaluate whether random mtDNA mutations precede and drive pathogenic mutant populations in human cells, and (4) reduce mtDNA mutations in human cells. Our specific aims are feasible, because of our dramatic advance in our ability to sensitively measure mitochondrial mutations, and important, given the critical role of mitochondria in aging and cancer. A mechanistic understanding of the environmental factors that accelerate mtDNA mutation should aid in the identification of risk factors and methods that prevent and/or slow age-related debilitation and disease. Ultimately, fulfillment of our proposed aims will help unravel the role of mitochondrial mutagenesis in human aging and potentially aid in the amelioration of age-related disease, extending the number of healthy and active years of life.

Aaron Bowman
Vanderbilt University
"A Manganese-Handling Deficit in Huntington's Disease Selectively Impairs ATM-p53 Signaling"

The essential micronutrient manganese is enriched in the brain, especially the basal ganglia. We sought to identify neuronal signaling pathways responsive to neurologically relevant manganese levels, as previous data suggested manganese alterations occur in Huntington's Disease (HD). We found that p53 phosphorylation is highly responsive to manganese levels in human and mouse striatal-like neuroprogenitors. The Ataxia Telangiectasia Mutated (ATM) kinase is responsible for this manganese-dependent phosphorylation of p53. Activation of ATM-p53 by manganese was severely blunted by pathogenic alleles of *Huntingtin*. HD neuroprogenitors exhibited a highly manganese selective deficit in ATM kinase activation, since DNA damage and oxidative injury, canonical activators of ATM, did not show similar deficits. Manganese was previously shown to activate ATM kinase in cell-free assays. We found that human HD neuroprogenitors have reduced intracellular manganese with neurologically relevant manganese exposures. Pharmacological manipulation to equalize manganese between HD and control neuroprogenitors rescued the ATM-p53 signaling deficit.

Jared Brown

University of Colorado

"Nanoparticle-Immune Interactions from a Biophysical to Physiological Perspective"

Concern about the use of engineered nanomaterials (ENMs) has increased significantly in recent years because of potentially hazardous impacts on human health. Upon introduction into physiological environments ENMs associate proteins, lipids and macromolecules forming a "biocorona." The ENM-biocorona alters the ENM-cell interface resulting in modified uptake, activity, clearance, and toxicity. Here we characterized the formation of a complex ENM-biocorona (consisting of multiple proteins) on AgNPs and carbon nanotubes and examined its alterations in cellular interactions and protein structure and function. Secondly, we have examined the involvement of mast cells and the IL-33/ST2 axis in pulmonary, cardiovascular and *in vitro* responses to ENMs including multi-walled carbon nanotubes (MWCNT) and silver nanoparticles (AgNP). We have established that certain ENMs are capable of inducing mast cell degranulation *in vitro*. For example, AgNPs induce mast cell degranulation that is dependent upon interaction with scavenger receptor class B (SR-BI). Through use of hyperspectral darkfield microscopy and ICP-MS, we have observed direct interaction and uptake of AgNP by mast cells resulting in degranulation that is not dependent on dissolution. For *in vivo* studies, we have utilized mast cell deficient mice *(Kit$^{W\text{-}sh}$)* and ST2$^{-/-}$ or IL-33$^{-/-}$ mice to assess systemic and pulmonary inflammatory responses following ENM exposure. We have found that mice with normal mast cell populations exhibit significant ENM directed pulmonary inflammation, impaired lung function, altered systemic T cell populations and presence of mast cell products. In contrast, these toxicological effects of ENMs were not observed in mice deficient in mast cells *(Kit$^{W\text{-}sh}$)* or mice with mast cells unable to respond to IL-33 (ST2$^{-/-}$ mast cell reconstituted *Kit$^{W\text{-}sh}$* mice or IL-33$^{-/-}$ mice). In addition, we have observed a role for SR-BI in mediating lung inflammation in mice following ENM instillation. Our findings establish that biocorona formation, mast cells, the IL-33/ST2 axis and SR-BI all contribute to adverse immune effects to ENMs giving insight into a unique mechanism of toxicity. This work was supported by NIEHS R01 ES019311 and U19 ES019525.

Brent Carter

University of Iowa Carver College of Medicine

"Modulation of the Mevalonate Pathway by Akt Controls Macrophage Survival and Development of Pulmonary Fibrosis"

Protein kinase B (Akt) is a key effector of multiple cellular processes, including cell survival. Akt, a serine/threonine kinase, is known to increase cell survival by regulation of the intrinsic pathway for apoptosis. In this study, we found that Akt modulated the mevalonate pathway, which is also linked to cell survival by increasing Rho GTPase activation. Akt modulated the pathway by phosphorylating mevalonate diphosphate decarboxylase (MDD) at Ser. This phosphorylation in macrophages increased activation of Rac1, which enhanced macrophage survival because mutation of MDD (MDD_{S96A}) induced apoptosis. Akt-mediated activation in macrophages was specific for Rac1 since Akt did not modulate other Rho GTP-binding proteins. The relationship between Akt and Rac1 was biologically relevant as Akt$^{+/-}$ mice had significantly less activated Rac1 in alveolar macrophages, and macrophages from Akt$^{+/-}$ mice had an increase in active caspase-9 and -3. More importantly, Akt mice were significantly protected from the development of pulmonary fibrosis suggesting that macrophage survival is associated with the fibrotic phenotype. These observations for the first time suggest that Akt plays a critical role in the development and progression of pulmonary fibrosis by enhancing macrophage survival via modulation of the mevalonate pathway.

Sarah Delaney

Brown University

"Inflammation as a Mediator of Dynamic DNA Mutations"

Triplet repeat sequences, such as CAG/CTG, expand in the human genome to cause several neurological disorders. Interestingly, the oxidatively damaged nucleobase 8-oxo-7,8-dihydroguanine (8-oxoG) has been implicated in triplet repeat expansion. Our overall objective is to define the molecular mechanism of CAG/CTG triplet repeat expansion and determine the extent to which 8-oxoG plays a role as the chemical founder event. We have identified a hot spot for DNA damage in the non-canonical structures adopted by CAG/CTG DNA, and performed a comprehensive kinetic analysis of base excision repair (BER) on these repetitive DNA substrates. These results have allowed us to propose a toxic cycle in which BER is initiated on triplet repeat sequences and damage accumulates in repair intermediates, resulting in an incremental expansion of the triplet repeat sequence. Recent work has begun to explore BER on CAG/CTG sequences in the context of nucleosome core particles.

Wenbin Deng

University of California-Davis

"Stem Cells for Neural Regeneration, Drug Discovery, and Toxicology Studies"

The brain has two major cell types: neurons and glia. Our view about how the brain works has been traditionally neuro-centric, even though glial cells significantly outnumber neurons. Emerging evidence indicates that glial cells are critical for many physiological, pathological, and toxicological processes in the nervous system. Using mouse models (genetically modified or surgically or chemically induced models) and human induced pluripotent stem cells, Deng lab conducts basic and translational research on glial cells in health and disease. In my talk, I will discuss our recent results on (1) the role of neuron-glia synapses in central nervous system (CNS) development and function, and excitotoxic, oxidative or inflammatory forms of injury to the CNS, (2) stem cell differentiation towards neuronal and glial lineages for CNS regeneration, drug discovery, and toxicology studies.

Rebecca Fry

University of North Carolina-Chapel Hill

"Prenatal Arsenic Exposure, Shifts in Cell Signaling Pathways and Newborn Health Effects"

Exposure to inorganic arsenic (iAs) early in life is associated with adverse health effects in infants, children, and adults, and yet the biological mechanisms that underlie these effects are understudied. The objective of this research was to examine the both transcriptomic and proteomic shifts associated with prenatal iAs exposure using cord blood samples isolated from newborns from Gómez Palacio, Mexico. Genomic signaling was observed to be associated with innate and adaptive immunity, under the regulation of a core set of miRNAs. A total of 111 proteins were identified that had a significant association between protein level in newborn cord blood and prenatal exposure to arsenic. Many of these proteins are regulated by tumor necrosis factor (TNF) and are enriched in functionality related to immune response/inflammatory response and cellular development/proliferation. Inter-individual differences in proteomic response were observed in which 30 newborns were "activators," displaying a positive relationship between protein expression and prenatal arsenic exposure. For 20 "repressor" newborns, a negative relationship between protein expression level and prenatal arsenic exposure was observed. The activator/repressor status was significantly associated with prenatal arsenic exposure and head circumference in newborn males. These results may provide a critical groundwork for understanding the diverse health effects associated with prenatal arsenic exposure and how inter-individual responses to arsenic may influence susceptibility to these effects.

Stacey Harper

Oregon State University

"Integrative Studies to Define Drivers of Nanomaterial Toxicity"

Understanding the inherent and conditional factors associated with nanomaterial toxicity is critical to the development nanotechnologies that pose minimal threats to humans and the environment over the life cycle of the nanomaterial. Currently, vast toxicological data gaps exist regarding the risks associated with nanomaterial exposure, and the principal characteristics that may be predictive of nanomaterial interactions with biological systems have yet to be identified due of this lack of information. Thus, rapid testing strategies are immediately necessary to identify the specific features of nanomaterials that result in toxicity in order to mitigate risks from exposure and define structure-property relationships that can be used to predict nanomaterial hazard *in lieu* of empirical data. We have compared the results of several different models built to predict toxicity from the open-source data on nanomaterial toxicity to embryonic zebrafish *(Danio rerio)* found in the Nanomaterial-Biological Interactions (NBI) knowledgebase at Oregon State University. Model comparisons included the ABMiner predictive models, MATLAB clustering analysis and the use of Self-Organizing Map (SOM) based consensus clustering conducted on the data in the NBI knowledgebase (nbi.oregonstate.edu). Overall results suggest that exposure concentration and outermost surface chemistry (and thus surface charge) both should be considered in conjunction with the core composition of nanomaterials when trying to develop predictive models for developing zebrafish. Thus, classification of nanomaterials by simple descriptors such as core composition may not be sufficient for predicting nanomaterial toxicity or managing nanomaterial risks. Computational analysis of the data from OSU's Nanomaterial-Biological Interactions knowledgebase has revealed that surface chemistry is one of the key features that determine nanomaterial toxicity.

Yu-Ying He
The University of Chicago
"Mechanism of UVA-Induced Skin Cancer"

Melanoma and non-melanoma skin cancer (NMSC) are among the most common cancers causing serious morbidity and mortality, and is on the rise for the past decades. Their shared, major environmental risk factor is ultraviolet (UV) radiation from sunlight and artificial sources, including both UVB and UVA. As compared with UVB, UVA has long been understudied for its contribution and mechanistic action in skin cancer. Our long-term goal is to establish new molecular targets for developing improved preventive and therapeutic strategies for NMSC and melanoma. Here we show that in both primary human melanocytes and keratinocytes, UVA regulates p62, the selective autophagy adaptor and substrate. In a xenografted melanoma mouse model, p62 addition increases tumor formation while p62 knockdown decreases it. p62 is up-regulated in human skin tumors and human melanoma cells. p62 binds with the oncogenic transcription factor Twist1, and increases Twist1 stability and activity through both autophagy and proteasome mechanisms. These findings imply that p62 plays a critical role in UVA-induced tumorigenesis of both melanoma and NMSC.

Sven-Eric Jordt
Duke University School of Medicine
"Sensory TRPA1 Channels Control Inflammation and Pruritogen Responses in Allergic Contact Dermatitis"

Allergic contact dermatitis is a common skin disease associated with inflammation and persistent pruritus. Transient Receptor Potential (TRP) ion channels in skin-innervating sensory neurons mediate acute inflammatory and pruritic responses following exogenous stimulation, and may contribute to allergic responses. Genetic ablation or pharmacological inhibition of TRPA1, but not TRPV1, inhibited skin edema, keratinocyte hyperplasia, nerve growth, leukocyte infiltration and antihistamine-resistant scratching behavior in mice exposed to the haptens, oxazolone and urushiol, the contact allergen of poison ivy. Hapten-challenged skin of TRPA1-deficient mice contained diminished levels of inflammatory cytokines, nerve growth factor and endogenous pruritogens such as Substance P (SP) and serotonin. TRPA1-deficient sensory neurons were defective in SP signaling, and SP-induced scratching behavior was abolished in Trpa1-/- mice. SP receptor antagonists such as aprepitant inhibited both hapten-induced cutaneous inflammation and scratching behavior. These findings support a central role for TRPA1 and SP in the integration of immune and neuronal mechanisms leading to chronic inflammatory responses and pruritus associated with contact dermatitis.

James Luyendyk
Michigan State University
"Hepatoprotective Effects of Fibrin(ogen)-Integrin Engagement in Liver Injury and Fibrosis"

Chronic liver damage in both humans and mice is associated with increased activity of the coagulation protease thrombin, and deposition of its substrate fibrin(ogen) in the liver (i.e., as a fibrin clot). Strong evidence indicates that thrombin promotes liver fibrosis through activation of protease activated receptor-1 (PAR-1). Historically, fibrin(ogen) deposition in the liver has also been presumed to contribute to disease. However, very few, if any studies have truly determined the role of fibrin(ogen) in chronic liver injury and fibrosis. Applying a mouse model of chronic xenobiotic-induced biliary fibrosis, which recapitulates many features of primary sclerosing cholangitis, we have uncovered mechanisms whereby fibrin(ogen) inhibits chronic liver injury and biliary fibrosis. Utilizing a combination of mice lacking fibrin(ogen), mice expressing mutant fibrin(ogen) proteins, and FDA-approved antifibrinolytics, we have mapped a mechanism whereby fibrin(ogen) engagement of both platelet and leukocyte integrins inhibits the progression of liver fibrosis caused by chronic biliary injury. Although the role of fibrin(ogen) and these cell types in liver fibrosis is most certainly context-dependent, our results call into question the assumption that fibrin(ogen) is universally detrimental in chronic liver disease.

Scott McCulloch

North Carolina State University

"Preventing Mutations by Making Mutations – Investigating the Molecular Mechanism of Translesion Synthesis by Human DNA pol η"

Oxidative stress can be caused by many common environmental exposures, such as polycyclic aromatic hydrocarbons, heavy metals, pesticides, as well as ultraviolet and ionizing radiation. Reactive oxygen species are created by normal cell processes oxidative stress is defined by an excess of them relative to protective, antioxidant compounds. They can cause multiple types of DNA lesions, the most common being 8-oxo-guanine (8-oxo-dG). If left unrepaired, this lesion is highly mutagenic, base pairing with adenine in a Hoogsteen fashion that can escape detection by the proofreading activity of the replicative polymerases. Translesion synthesis (TLS) of damaged bases by specialized polymerases allows completion of DNA replication in the face of lesions that would otherwise cause collapse of the stalled the replication fork. This can ultimately lead to strand breaks and other gross chromosomal changes. TLS past several DNA lesions by Y-family members occurs with higher efficiency compared to replicative polymerases, making them the preferred choice for ensuring replication is completed, even though the fidelity of many TLS polymerases is relatively low. We have previously demonstrated that human pol eta performs efficient bypass of 8-oxo-dG, but also observed that the bypass occurred with remarkably low fidelity. Errors were generated during ~50% of all bypass events. As expected, the most frequent error was adenine misinsertion opposite 8-oxo-dG. This implies that if pol eta suppresses mutagenesis during 8-oxo-dG bypass the fidelity must be substantially altered somehow. We aim to determine which factors may influence the fidelity of the bypass reaction and also to determine what role, if any, pol η plays in the generation of mutations during times of oxidative stress when the number of 8-oxo-dG bypass events would be greatly elevated. The goals of these projects include: 1) to determine the effects of replication proteins on the efficiency and fidelity of 8-oxo-dG bypass by human pol η; 2) to identify and characterize human pol η mutants, including known SNPs, that display altered fidelity for 8-oxo-dG bypass; and 3) to determine the mutation rate of wild type and pol η deficient cells, and cells expressing mutant forms of pol η, under conditions of oxidative stress, including environmentally relevant doses of UVB and UVA. The long term objectives of this proposal are to determine the molecular mechanisms that modulate the efficiency and fidelity of 8-oxo-dG bypass in human cells, and ultimately the mutagenesis caused by oxidative DNA damage.

Joel Meyer

Duke University

"Fate and Effects of Persistent Mitochondrial DNA Damage"

Mitochondrial DNA (mtDNA) is more sensitive than nuclear DNA to many common genotoxins, and lacks some repair pathways that are present in the nucleus. In particular, damage formed after exposure to environmentally important genotoxins such as ultraviolet C (UVC) radiation and some polycyclic aromatic hydrocarbons and mycotoxins is not repaired in mtDNA. We are studying the fate and effects of such damage using the nematode model *Caenorhabditis elegans* as well as cell culture. We hypothesized that the effects of such damage would be particularly important after early life stage exposure since mtDNA copy number is lowest at that time. We found that UVC-induced photodimers result in lower levels of mtDNA-encoded mRNAs, decreased ATP levels, decreased oxygen consumption, larval developmental arrest, and dopaminergic neurodegeneration. Some of these effects are persistent throughout life, including a large decrease in steady-state ATP levels even at exposure levels that do not affect lifespan. We are currently investigating the mechanism responsible for this lifelong effect. We also found that UVC-induced mtDNA damage is slowly removed in a process dependent at least in part on mitochondrial fusion, fission and autophagy, and are investigating whether this process is one of general autophagy or targeted mitophagy. Finally, we are testing the hypothesis that mutations in mitochondrial fusion, fission and autophagy genes (including the Parkinson's Disease-related genes PINK1 and PARKIN) alter the effects of persistent mtDNA damage.

Gokhan Mutlu

The University of Chicago

"Role of β_2-adrenergic Receptors in Particulate Matter-Induced Lung Inflammation and Thrombosis"

The mortality associated with acute exposure to ambient particulate matter (PM) is largely due to an increased incidence of acute thrombotic cardiovascular events; however, the mechanisms explaining this association are incompletely understood. We have previously shown that the release of interleukin-6 (IL-6) from alveolar macrophages is required for a prothrombotic state and acceleration of thrombosis following exposure to PM. An additional mechanism linking PM exposure with cardiovascular events has been described by several groups of investigators who have observed changes in heart rate variability or peripheral vasoreactivity following exposure to PM and inferred from these data that PM-induced activation of the sympathetic nervous system might induce coronary vasoconstriction or arrhythmias. However, the effect of PM on sympathetic nervous system has not been directly investigated and the consequences of sympathetic nervous system activation on lung inflammation and thrombosis are not known. We have recently shown that PM exposure results in the systemic release of catecholamines, which engage the β_2-adrenergic receptor (β_2AR) on murine alveolar macrophages to augment the release of IL-6. In mice, this promotes the development of a prothrombotic state sufficient to accelerate arterial thrombosis. In human alveolar macrophages, the administration of a β_2AR agonist augments, and a β-blocker inhibits PM-induced IL-6 release. Genetic loss or pharmacologic inhibition of the β_2AR on murine alveolar macrophages attenuates PM-induced IL-6 release and prothrombotic state. Exogenous β_2AR agonist therapy further augments these responses through a mechanism that requires the generation of ROS from mitochondria. These results provide a mechanistic paradigm linking activation of the sympathetic nervous system with metabolism, lung inflammation and an enhanced susceptibility to thrombotic cardiovascular events.

Timothy Nurkiewicz

West Virginia University School of Medicine

"Nanomaterial Inhalation Exposure and Microvascular Endpoints: Our Journey from an Obscure Skeletal Muscle to the Fetus"

For well over a decade, the association between pulmonary particle exposure and cardiovascular dysfunction has been known, yet the exact mechanisms linking exposure and effect have been unclear. Eight years ago, our initial hypothesis was that inflammatory mechanisms govern the systemic microvascular dysfunction that follows ultrafine particulate matter exposure, and the severity of this dysfunction is augmented in clinically relevant populations. We exposed rats and mice (male/female, young/adult) to experimental atmospheres relevant to environmental and occupational conditions. These atmospheres employed inhalable particle surrogates such as nano-titanium dioxide (nano-TiO_2). The primary particle size was ~21 nm; aerosol concentration ranged from 0 to 6 mg/m3; and exposure duration was typically 4-6 hours (sometimes being repeated up to eight times). Following inhalation exposure, intravital microscopy studies with the spinotrapezius muscle, and isolated arterioles from various organs were performed. Endothelium dependent arteriolar dilation was significantly impaired after nano-TiO_2 exposure, and this was accompanied with widespread venular leukocyte trafficking (rolling, adhesion, extravasation). Cellular changes in the microvascular wall that supported these observations included: oxidative and nitrosative stress; myeloperoxidase deposition, and decreased nitric oxide bioavailability. Neurogenic and metabolic impairments also occurred. Gender (female) and age (young) imparted partial protection against most of these extrapulmonary effects. Surprisingly, we also discovered that the lung was not a requirement for these microvascular effects in that introduction of nano-TiO_2 via the gut or tail vein also impaired reactivity. Given these discoveries of gender-based vasoprotection, and a total dearth of understanding about the fetal effects of maternal nanomaterial exposure, we developed our current hypothesis: ENM type and exposure route dictate the mechanism and severity of resultant microvascular dysfunction; and this dysfunction has dire consequences on maternal and fetal outcomes. In our first studies, we have shown that nanomaterial inhalation during the second half of gestation significantly impairs uterine microvascular function, and this decreases litter size and pup mass. Further, the pups display not only impaired reactivity, but also sensitivity to later exposures, and cognitive behavioral deficits (spatial navigation memory). Epigenetic and mechanistic studies are underway to fully reveal the underlying physiologic changes/consequences that follow maternal nanomaterial exposures.

Patricia Opresko

University of Pittsburgh Graduate School of Public Health

"Mechanisms of Telomere Damage and Repair"

Telomeres preserve genome stability, survival, and proliferation on a cellular level, and prevent degenerative diseases and cancer on an organism level. Critically short or aberrant telomeres trigger cell senescence or cause chromosome end-to-end fusions. Telomeric repeat sequences are highly susceptible to DNA damage. We found previously that the environmental genotoxicant hexavalent Cr(VI) induces telomere aberrations and damage. Cr(VI) generates bulky DNA adducts which are repaired by nucleotide excision repair (NER). A previous report that ultraviolet (UV) light-induced DNA photoproducts persist at telomeres suggested that NER is suppressed telomeres. NER removes a wide variety of DNA adducts generated by environmental genotoxicants and anti-cancer drugs, and is essential for preventing sun light induce skin cancers and alterations. Our goals are to examine NER enzyme activity at telomeres in cells and biochemically *in vitro*, and to define the impact of UV irradiation and Cr(VI) exposures on telomere structure and function in cells that are proficient and deficient for NER. Using a novel assay we discovered that UV photoproducts are removed in the bulk of telomeres derived from normal human fibroblasts, and that complete repair required 48 hours. However, UV exposure also induced telomere aberrations and telomere loss that appeared to result from failures in telomere replication. Cellular defense against UV photoproducts also requires translesion DNA synthesis; a process that enables bypass of blocking DNA lesions to complete genome duplication, so the lesions can be repaired after DNA replication. We uncovered new evidence that translesion DNA synthesis is required for telomere preservation following genotoxic exposure to UV irradiation and Cr(VI) exposures. Understanding how telomeres are damaged and repaired will be useful for advancing therapies that 1) preserve telomeres to maintain healthy cells and tissue after genotoxic exposures, or that conversely 2) deplete telomeres to arrest proliferating cancer cells.

Jill Poole

University of Nebraska Medical Center

"The Role of Pattern Recognition Receptors in Organic Dust-Induced Airway Inflammation"

Exposure to complex organic dusts in the agricultural industry, particularly from large animal farming environments, results in an increased risk of developing significant chronic airway diseases. A challenge in defining mechanisms of organic dust-induced inflammatory responses is in the inherent complexity of the dust. We utilized an animal model of inflammatory lung injury to delineate the functional roles of specific components (bacterial lipopolysaccharides [LPS] and peptidoglycans [PGN]) within these complex organic dusts from large animal farm confinements and to provide underlying mechanistic insights. During this funding period, we initiated a paradigm shift in this field by finding that gram-positive bacterial PGNs, as opposed to gram-negative LPS, were the predominant drivers of lung inflammatory consequences, with a strong role demonstrated for the Toll-like receptor 2 (TLR2) signaling pathway. We also defined roles for several other pattern-recognition receptor pathways including TLR4, TLR9, nuclear oligomerization domain molecule 2 (NOD2), IL-18R (but not IL-1R), and scavenger receptor A (SRA/CD204). The strongest phenotype discovered was for the common TLR/IL-1R adaptor protein, MyD88. Whereas neutrophils dominate airway responses to organic dust, we defined roles for $\alpha\beta$-expressing $CD4^+$ T cells, a Th1/Th17 lung microenvironment, and activated $CD11c^{hi}CD11b^{hi}$ lung macrophages. Because agricultural workers have a very high prevalence of musculoskeletal disease, our research has evolved to understand the systemic consequences of these inhalant exposures on bone homeostasis. Importantly, using state-of-the-art micro-CT imaging we discovered significant bone loss following repetitive treatment with inhalant organic dust and its critical components, which established for the first time, an animal model connecting inhalant lung injury to bone loss. Collectively, these observations could lead to novel therapeutic targets to prevent and/or reduce lung and systemic disease manifestations as well as to the future importance of environmental sampling strategies.

Christina Porucznik

The University of Utah School of Medicine

"Periconceptional Exposure Assessment – Progress and Preliminary Findings"

Human and animal evidence suggests that periconceptional exposures may have short- and long-term health effects. We are recruiting a preconception cohort of couples with normal or unknown fertility status living in the greater Salt Lake City area for the Home Observation of Periconceptional Exposures (HOPE) Study. The couples learn a simple fertility awareness method in order to identify their fertile window and self-collect numerous biospecimens timed to the woman's ovulation. Recruitment has been open for two years, and we have enrolled 140 of our 300 couple goal, with 83 couples achieving pregnancy (as of June 2, 2014). 43 percent of the pregnant couples conceived in cycle 1 or 2 of participation, and we have periconceptional urine and saliva specimens from both partners as well as a semen specimen. Specimen collection compliance is approximately 90 percent. Recruitment and analysis are ongoing. We report preliminary findings in this abstract.

BPA has been detected in 100 percent of urine specimens at >=0.4 ng/mL. BPA levels in males are higher than in females. Daily variability in BPA is high. We estimate that approximately five consecutive daily samples are required in order to classify correctly a female participant with high BPA exposure with 81 percent sensitivity and 90 percent specificity. We have also identified seasonality in BPA and trichloroacetic acid (TCAA, a disinfection byproduct) exposure with different means in the population by month.

The primary hypothesis is that time to pregnancy will be longer for couples in which the male partner has higher exposure to BPA. Preliminary, unadjusted, results from the first 52 pregnancies demonstrate no relationship between BPA exposure and time to pregnancy. However, we have identified a relationship between male BPA exposure and semen quality. For every unit increase in BPA geometric mean, the odds of abnormal concentration increased by 1.18 (95% CI 1.01, 1.37). Men in the high BPA tertile (≥4.67 ng/mL) had a 3.30 (95% CI 1.02, 10.70) increased odds of abnormal sperm heads compared to men in the low BPA tertile (≤1.90 ng/mL). Among the first 32 births, we noted variability in the time from delivery to achievement of lactogenesis II, and we plan to investigate the association between maternal levels of BPA at conception and the time to onset of lactogenesis II.

These preliminary findings will be presented at the Society for Pediatric and Perinatal Epidemiologic Research in June 2014 and at the International Society for Environmental Epidemiology Conference in August 2014.

Jason Richardson

Rutgers Robert Wood Johnson Medical School

"Translational Studies on the Role of Developmental Pyrethroid Exposure in ADHD: Experience with the ViCTER Mechanism"

Attention-deficit hyperactivity disorder (ADHD) is a clinically heterogeneous disorder characterized by core features of impulsivity, hyperactivity, and attention deficits, which is estimated to affect 8-12 percent of school-aged children worldwide. While ADHD is a complex disorder with significant genetic contributions, no single gene has been linked to a significant percentage of cases, suggesting that environmental factors or gene-environment interactions may contribute to the etiology of ADHD. Several environmental factors have been identified as potential risk factors for ADHD, including prenatal exposure to alcohol, tobacco, and lead. However, studies of environmental risk factors for ADHD have been hindered by the difficulties of quantifying environmental exposures in humans along with the impossibility of conducting experimental exposures of humans due to ethical considerations. To advance progress in this area, the goal of the current application is to develop a "Virtual Consortium" between experts in neurotoxicology (Dr. Richardson), ADHD genetics (Dr. Faraone), and environmental epidemiology and children's health (Drs. Yolton, Lanphear and Froehlich) to promote translational research exploring the relationship between developmental pyrethroid exposure and ADHD. This application builds on Dr. Richardson's current grant entitled "Mechanisms of Pesticide-Induced Neurobehavioral Deficits: Relevance to ADHD." *Data generated from this grant has demonstrated that developmental exposure of mice to the pyrethroid pesticide deltamethrin produces neurochemical and behavioral dysfunction similar to that observed in ADHD patients. Furthermore, epidemiological data reveal that elevated urinary pyrethroid metabolite levels in children increases risk of ADHD diagnosis in children 2.3-fold.* The ViCTER project sought to identify alterations in gene expression in an animal model of ADHD based on developmental pesticide exposure, validate these molecular biomarkers in samples from a well characterized cohort of ADHD patients, and to test the association between urinary pesticide metabolite levels, gene expression changes, and behavioral alterations in children 5 years of age from an ongoing prospective birth cohort. Along with data, our experience with the ViCTER mechanism and moving from basic to translational research will be discussed.

Joseph Shaw

Indiana Unversity

"Effects of Environmental Contamination on Gene Copy Number Variation: Molecular Blueprint for Adaptation, Susceptibility, and Disease"

Understanding inter-individual variation in response to environment stress is important for human health, because it defines susceptibility. These differences in response are described by variation in environments, and genomes that combine to give rise to phenotypic variation within populations. In this talk we draw from recent population genomic studies to explore how toxicant exposure contributes to genome variability, influences the fate of genome variation in populations, and over micro-evolutionary time scales drives population-level outcomes. These studies contribute to and make use of a maturing genomic tool kit for Daphnia pulex, that includes array comparative genomic hybridization (aCGH), full-genome re-sequencing of more than 50 individuals, and both neutral and selection driven mutation accumulation lines. We demonstrate the benefits of the Daphnia mutation model reporting that the spectrum of neutral structural mutations observed in Daphnia more closely resembles the complexity of structural mutations observed in humans – especially those associated with disease, because they capture large-scale gene conversions, duplicates and deletions that are absent in fly, worms, and yeast. We further demonstrate that structural mutations contribute more to evolution than base-substitutions. Using the Daphnia model we discover exposure-induced alterations in the magnitude and distribution of gene copy number (CNV). We reveal a method for measuring the contribution of this environment induced genome variation on phenotype, and through spatial and temporal studies determine that CNV play a major role in establishing the environmental stress-response of a population. Finally, we discuss the importance of understanding genome variation and the evolutionary forces that shape it to the applied goals of environmental health protection.

Angela Slitt

University of Rhode Island

"Going Beyond the Antioxidant Response: Nrf2 as a Metabolic Regulator"

Childhood obesity and diabetes is on the rise in the United States, with an estimated 20 percent of 6- to 11-year-olds being categorized as obese. The CDC estimates that more than 86 percent of U.S. adults will be overweight or obese, and more than 50 percent obese by the year 2030. A major complication of obesity and insulin-resistance is NAFLD, and trends have increased in children over the past 20 years. With no intervention, NAFLD can progress to NASH and cirrhosis, with an exponential decrease in liver function. Liver steatosis is caused by upregulation of several transcriptional pathways, which promote lipid accumulation and synthesis such as Ppar-γ and Srebp-1, as well as down regulation of fatty acid oxidation regulators such as Sirtuin deacetylases and AMP-Kinase. The Nrf2-Keap1 pathway is well described regarding the transcriptional activation of cytoprotective genes, resulting in enhanced antioxidant capacity which is cytoprotective, but our data demonstrate that Nrf2 can promote hepatic steatosis in mice through enhancing Ppar-gamma mRNA expression and Nrf2-null mice have decreased NADPH, a reducing equivalent needed for lipid storage as triglycerides. Additional data demonstrate that the Sirtuin-1 (Sirt1) deacetylase, which protects against steatosis, negatively regulates hepatic Nrf2 activity *in vivo*. This presentation will discuss obesity how modulation of Nrf2 expression in in vivo systems affects hepatic steatosis induced by obesity, diet, and fasting.

Alexander Star

University of Pittsburgh

"Investigation and Mitigation of Carbon Nanomaterial Toxicity"

Because of the unique properties of carbon nanotubes (CNTs), such as small size, large surface area, high strength, and electrical conductivity, this carbon nanomaterial has been widely used in high performance composites, electronics, and medical therapeutics. The current level of large-scale production of CNTs has reached several thousand tons per year and is projected to grow in the foreseeable future. With such a large amount of CNTs being produced and the handling involved during their processing, workers increase their risk of point-source exposure through inhalation, and the general community is at risk of the potential toxic effects of CNT-containing products. Biopersistence of CNTs has been long viewed as the major factor contributing to the toxic effects of these nanomaterials in the body. We, however, hypothesized that CNTs may undergo enzymatic oxidation and biodegradation *in vivo*. Our results have demonstrated that the plant peroxidase, horseradish peroxidase (HRP), and the animal peroxidase, myeloperoxidase (MPO), catalyze the oxidation/biodegradation of carbon nanomaterials, particularly single-walled carbon nanotubes (SWCNTs). In the mechanistic investigations, we demonstrated that only SWCNTs that contain oxygen moieties and defect sites undergo enzymatic degradation; pristine SWCNTs were not observed to degrade over the same time period. In the cellular studies, we showed that short-cut carboxylated SWCNTs could be degraded by neutrophils, inflammatory cells containing high concentrations of MPO. *In vivo* studies demonstrated that inflammatory response in MPO-knockout (k/o) mice (i.e., mice with MPO deficiency) was stronger than that in wild-type mice and CNT degradation and clearance from the lungs of MPO k/o animals was markedly less effective. More recently, we have also shown that the CNT biodegradation process can take place with eosinophil peroxidase (EPO) and macrophages, which are relatively poor in MPO, but utilize a different oxidizing system such as peroxynitrite generators. The discovery of the enzymatic CNT degradation processes opens new opportunities for the regulation of CNT distribution and fate *in vivo* by controlling inflammatory response and/or employing CNT-metabolizing enzymes. These findings are also applicable to applications of CNTs in nanomedicine as drug delivery vehicles, where biodegradation may either catalyze the release of the cargo conjugated to the CNT carrier or destroy the CNT delivery vehicle post-release thereby mitigating potential toxicity.

Vishal Vaidya

Harvard Medical School

"Modernizing Toxicology: Biomarkers and Cell-Based Approaches to the Rescue"

Biomarkers have tremendous transformative potential in translational medicine to not only monitor the efficacy and safety of a therapeutic but also to guide the diagnosis of a disease, determine risk of developing diseases and to inform treatment options. In this presentation I will highlight the success of our laboratory in collaboration with Predictive Safety Testing Consortium that led to the qualification of Kidney Injury Molecule-1 (Kim-1) as a biomarker for kidney toxicity monitoring by regulatory agencies. We were able to characterize the performance of Kim-1 as a biomarker from preclinical and clinical evaluation to regulatory qualification and point-of-care testing. More recently, we have also uncovered the key transcription factor and kinase regulating Kim-1 expression in the kidney. In addition, I will provide an update on identification and evaluation of alternative mechanistic and translational biomarkers for kidney disease such as fibrinogen and urinary microRNAs. The second approach in modernizing toxicology that is aligned with the Tox21 initiative aims towards transforming the traditional *in vivo*, dose-response based safety assessment by developing high throughput cell-based assays. I will describe our ongoing efforts that use primary human proximal tubular epithelial cells in an attempt to develop multi-dimensional toxico-response signatures that represent a biography of the toxic cell.

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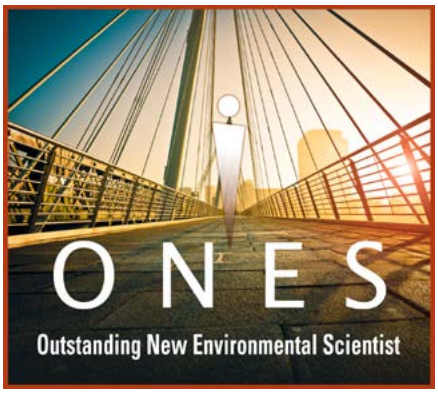

Biographies

Lauren Aleksunes
Rutgers University

Lauren Aleksunes' research focuses on how transporters regulate chemical exposure in the kidneys, placenta, liver, and brain. Aleksunes was recently promoted to associate professor in the Ernest Mario School of Pharmacy at Rutgers University. She is also a resident scientist in the Environmental and Occupational Health Sciences Institute. She received her Ph.D. in Pharmacology and Toxicology from the University of Connecticut in 2006 with Jose Manautou and was a postdoctoral fellow at the University of Kansas Medical Center from 2007-2009 with Curt Klaassen. In 2009, Aleksunes joined Rutgers, where her research interests continued in drug metabolism and transport of toxicants in the placenta, liver, kidneys, and brain. In 2010, she was selected as an Outstanding New Environmental Scientist Awardee from NIH/NIEHS. Aleksunes has more than 65 publications, including peer-reviewed research articles, invited reviews, and book chapters and is currently on the editorial board of four toxicology journals. Her laboratory is funded by two R01 grants from NIH/NIEHS and an R21 grant from NIH/NIDDK. She is also an active member of the Society of Toxicology and the American Society for Pharmacology and Experimental Therapeutics.

Jason Bielas
Fred Hutchinson Cancer Research Center

Jason Bielas is an associate member in the Translational Research Program at Fred Hutchinson Cancer Research Center (FHCRC) and holds an Affiliate Associate Professorship in Department of Pathology at the University of Washington. Bielas has had a long-standing interest and commitment to discerning the relationship between mutagenesis, aging, and cancer. Bielas earned his Ph.D. with Distinction and the Governor General of Canada's Gold Medal in 2004 from the Department of Biology at York University in Toronto. Together with doctoral thesis advisor, John Heddle, he developed novel methods to measure DNA repair and mutation to delineate the relationship between proliferation and mutagenesis. Following his doctoral work, Jason pursued postdoctoral training in the laboratory of Dr. Lawrence A. Loeb. At the University of Washington, Bielas' primary research focused on the role of a mutator phenotype in carcinogenesis. He continued to develop novel methods to monitor mutagenesis, including the Random Mutation Capture (RMC) assay, which demonstrates that tumors exhibit point mutation instability (PIN) and that mitochondrial point mutations do not limit natural lifespan. During his tenure as graduate student and postdoctoral fellow, Bielas received a number of awards, including a graduate scholarship from the Natural Sciences and Engineering Research Council of Canada (NSERC), an Ontario Graduate Scholarship in Science and Technology, the RH Haynes Scholarship for Academic Excellence, and Postdoctoral Fellowships from NSERC, the Canadian Institutes of Health Research, and the Terry Fox Foundation. Since opening his laboratory at the FHCRC, Bielas has received a New Scholar Award from the Ellison Medical Foundation, a New Investigator Award from the Department of Defense, and an Outstanding New Environmental Scientist (ONES) (RO1) Award from the National Institute of Environmental Health Sciences.

Aaron Bowman
Vanderbilt University

Aaron Bowman, Ph.D., is an assistant professor in the Department of Neurology at Vanderbilt University. He is also an investigator in the Vanderbilt Kennedy Center for research on Human Development. In addition, he holds appointments in the Vanderbilt Center for Molecular Neuroscience, Vanderbilt Center in Molecular Toxicology, and Vanderbilt Center for Stem Cell Biology. Bowman received his Ph.D. in biomedical sciences in 2000 from the University of California San Diego. He did postdoctoral fellowship training at Princeton University and Baylor College of Medicine. Bowman is a 2008 recipient of the Outstanding New Environmental Scientist (ONES) RO1 award from the National Institute of Environmental Health Sciences. In 2012, Bowman was elected Vice-president Elect of the Neurotoxicology Specialty Section (NTSS) of the Society of Toxicology (SOT) in 2012, a four-year term and currently serves as president of NTSS. He also served as the senior councilor of the Stem Cells Specialty Section of SOT in 2012. Bowman also serves on the editorial boards of NeuroToxicology, BMC Pharmacology and Toxicology, as well as performing other ad hoc editorial and peer review services.

The goal of Bowman's research is to define mechanisms of neuronal dysfunction and understand the basis of selective neuropathology by characterizing the molecular function of disease genes and their interaction with environmental toxicants under both normal and pathological conditions. His work is supported by two RO1 grants focused on the influence of manganese exposure in Huntington's disease (ES016931, PI) and Parkinson's disease (ES010563, MPI). Furthermore, he is a co-recipient of a NIEHS ViCTER RO1 (ES010563-13S1, MPI) examining a role for manganese in restless legs syndrome. His lab uses patient-specific induced pluripotent stem cells, high throughput screening, mouse models and biochemical approaches to examine gene-environment interactions in neurological disease.

Jared Brown
University of Colorado

Jared Brown is an assistant professor and director of the Toxicology Graduate Program in the Department of Pharmaceutical Sciences at the University of Colorado Anschutz Medical Campus. Before joining the faculty at the University of Colorado in 2013, Brown was an assistant professor at the Brody School of Medicine at East Carolina University in the Department of Pharmacology and Toxicology. He received his doctorate in toxicology from the University of Montana and was a postdoctoral fellow in the Laboratory of Allergic Diseases at the National Institute of Allergy and Infectious Disease at the National Institutes of Health. Brown's research interests are to understand nanoparticle-immune interactions particularly as it relates to the development of allergic disease. Brown is author or co-author on more than 50 peer-reviewed publications, review articles, and book chapters and has served on multiple study sections for NIH, FDA, NIOSH, and several EU funding agencies related to nanoparticle toxicity. Brown was a recipient of the Outstanding New Environmental Scientist Award in 2010. In addition, Brown serves as a project director on an NIEHS funded Center for Nanotechnology Health Implications, and he was a participant in the NIEHS NanoGo consortium. Brown has been an active member of the Society of Toxicology since 2000 and is currently councilor for the Nanotoxicology Specialty Section. In addition, Brown is a member of the American Thoracic Society and American Association of Immunologists.

Brent Carter
University of Iowa Carver College of Medicine

Brent Carter is a professor of internal medicine at the University of Iowa Carver College of Medicine. The primary goal of his research is to understand the molecular mechanisms that modulate the development of lung injury and pulmonary fibrosis from occupational and environmental exposures. Specifically, Carter's laboratory focuses on the role of macrophage-derived oxidant production and signaling in the pathogenesis of pulmonary fibrosis. They have found that mitochondrial-derived oxidative stress in alveolar macrophages is critically linked to the fibrotic phenotype. Investigations include basic *in vitro* studies to uncover mechanisms using a genetic approach in order to manipulate the oxidant signaling. The *in vitro* studies are translated *in vivo* in a murine model using transgenic animals. Finally, the observations are then verified in alveolar macrophages from patients with asbestos-induced pulmonary fibrosis.

Sarah Delaney
Brown University

Sarah Delaney received her B.A. in Chemistry from Middlebury College in 1999 and Ph.D. in Chemistry from the California Institute of Technology in 2004, working in the laboratory of Jacqueline Barton. Dr. Delaney was a Damon Runyon postdoctoral fellow in the laboratory of John Essigmann at the Massachusetts Institute of Technology until 2007. Dr. Delaney is currently an Assistant Professor in the Department of Chemistry at Brown University. Her laboratory is focused on understanding the role of oxidation of DNA nucleobases in expansion of genetically unstable trinucleotide repeat sequences such as CAG/CTG. She teaches *Organic Chemistry, Chemical Biology*, and a First-Year Seminar *Kitchen Chemistry*. In 2010 she was awarded an Outstanding New Environmental Scientist (ONES) Award from NIH/NIEHS and in 2011 she received the Philip J. Bray Award for Excellence in Teaching in the Physical Sciences from Brown University.

Wenbin Deng
University of California-Davis

Wenbin Deng is a professor of biochemistry and molecular medicine at University of California, Davis. Before joining UC Davis, he was an instructor in neurology at Children's Hospital, Harvard Medical School. He received a Ph.D. in toxicology from Rutgers University and completed a postdoctoral fellowship in neuroscience at Harvard Medical School. Before coming to the United States, he completed his medical education and also earned a master's degree in pharmacology in China. Areas of research in Deng's lab include: (1) mechanisms of nervous system development, toxicity, and disease; and (2) adult (somatic) stem cells, induced pluripotent stem (iPS) cells and embryonic stem (ES) cells for disease modeling, drug discovery, and toxicology studies. Deng's lab performs genetic engineering, molecular and cellular imaging, platform technology, chemical toxicology, innovative pharmacology, and translational medical research. Deng has served on a variety of national/international panels and committees and organized/chaired a number of national/international conferences and symposia.

Rebecca Fry
University of North Carolina-Chapel Hill

Rebecca Fry is an associate professor in the Department of Environmental Sciences and Engineering at the Gillings School of Global Public Health at UNC-Chapel Hill. She also holds appointments in the curriculum in toxicology and the Lineberger Cancer Center. Fry received her Ph.D. in biology and completed her post-doctoral training in toxicogenomics. She leads one of three of the biomedical research projects within the UNC Superfund research program, where she is investigating the effects of prenatal cadmium exposure in populations in North Carolina. She is also funded by NIEHS to understand the health effects associated with prenatal arsenic exposure in a cohort in Mexico. Building off her expertise is in the areas of DNA repair, toxicogenomics, and systems biology, her research at UNC focuses on mechanisms of disease associated with toxic metal exposure early in life. A primary goal of Fry's research is to increase awareness of the deleterious impacts of exposures during the prenatal period and to improve public health initiatives to address this issue.

Stacey Harper
Oregon State University

Stacey Harper is an assistant professor of nanotoxicology in a joint position between the Department of Environmental and Molecular Toxicology and the School of Chemical, Biological and Environmental Engineering at Oregon State University (OSU). She is also a signature researcher at the Oregon Nanoscience and Microtechnologies Institute. In her laboratory, Harper employs *in vivo* approaches to evaluate the biological activity and toxic potential of novel nanomaterials, and has established a collaborative, multidisciplinary research program to develop a knowledgebase of Nanomaterial-Biological Interactions. She received her doctorate in Biological Sciences from the University of Nevada Las Vegas in 2003, was a postdoctoral fellow at the Environmental Protection Agency from 2003-2005, and an NIEHS postdoctoral scholar at Oregon State University from 2005-2009. From 2011-2012, Harper served as the president of the Pacific Northwest Association of Toxicologists, a regional chapter of the Society of Toxicology. Harper currently serves as the co-chair of ASTM International E56 Committee on Nanotechnologies and as a U.S. Delegate of ANSI-Accredited Technical Advisory Group for ISO/TC 229 on Nanotechnologies.

Yu-Ying He
The University of Chicago

Yu-Ying He is an assistant professor of medicine at the University of Chicago. She received her Ph.D. in chemistry in 2000 from the Chinese Academy of Sciences in China. Then she accepted the Humboldt Research Fellowship and spent one year at the University of Erlangen-Nuerenburg in Germany. In 2001, she came to NIEHS for her postdoctoral training with Colin Chignell. In 2007, she joined the faculty in the Department of Medicine at the University of Chicago. During her research career, Yu-Ying He has received several awards, including the first NIEHS Science Day Early Career Award, the NIH Fellows Award for Research Excellence (FARE), the American Skin Association Research Scholar Award, the American Cancer Society Research Scholar award, and the Outstanding New Environmental Scientist Award. Her research interests are in the genetic and environmental determinants of genomic stability using skin and skin cells as models.

Sven-Eric Jordt
Duke University School of Medicine

Sven-Eric Jordt is associate professor of anesthesiology at Duke University School of Medicine, where he relocated from Yale University in April 2014. He belongs to the first generation of ONES awardees, receiving the award in 2006. Research in the Jordt laboratory focuses on mechanisms of chemical sensing and their role in irritation, pain, and inflammation following environmental exposures. These efforts led to the discovery of TRP ion channels as key irritant sensors and drivers of inflammation and tissue injury, with implications for the development of countermeasures against chemical injuries, pain, pruritus, asthma, and smoking-induced morbidities. In addition to the ONES award, Dr. Jordt received the Presidential Early Career Award for Scientists and Engineers (PECASE) and other honors.

James Luyendyk
Michigan State University

James Luyendyk is an associate professor in the Department of Pathobiology and Diagnostic Investigation at Michigan State University. Jim received a B.S. in biochemistry from Colorado State University in 2000 and his Ph.D. in pharmacology/toxicology from Michigan State University in 2004. Jim was a postdoctoral fellow at the Scripps Research Institute from 2005-2007 and then joined the Department of Pharmacology, Toxicology and Therapeutics at The University of Kansas Medical Center, where he was an sssistant professor from 2007-2012. Research in Luyendyk's laboratory focuses on mechanisms coupling blood coagulation to the progression of acute and chronic liver disease.

Scott McCulloch
North Carolina State University

Scott McCulloch obtained his Ph.D. in toxicology at the University of Kentucky under the guidance of Guo-Min Li, investigating the mechanism of DNA mismatch and insertion/deletion loop repair. He then worked as a post-doctoral researcher under Thomas Kunkel at the National Institute of Environmental Health Sciences, studying the efficiency and fidelity of various polymerases when performing lesion bypass. He is currently an assistant professor at North Carolina State University in the Department of Biological Sciences, Program in Environmental and Molecular Toxicology. He is an associate member of the graduate school, precept in training grants to both the Program in Environmental and Molecular Toxicology and Biotechology programs, and a founding member of the Center for Human Health and the Environment. In addition to research, he teaches several undergraduate and graduate courses about fundamental, molecular, and environmental toxicology, and cancer biology.

Joel Meyer
Duke University

Joel Meyer received his B.S. from Juniata College in 1992, and then moved to Guatemala where he worked in a number of fields, including appropriate technology and high school teaching. He earned a Ph.D. in environmental toxicology from Duke University in 2003, and carried out postdoctoral research studying DNA damage and repair with Bennett Van Houten at NIEHS from 2003-2006. Meyer joined the Nicholas School of the Environment at Duke University in 2007, where he studies the effects of genotoxic agents and other pollutants on health. Meyer is interested in understanding the mechanisms by which environmental agents cause DNA damage, the molecular processes that organisms employ to protect prevent and repair DNA damage, and genetic differences that may lead to increased or decreased sensitivity to DNA damage. He is particularly interested in types of DNA damage that are not repaired in the mitochondrial genome, and is working to understand both the fate of such damage and its effects. Compounds of particular interest are polycyclic aromatic hydrocarbons, nanomaterials, and mitochondrial toxins. Most of his laboratory's current work is done with the model organism *Caenorhabditis elegans* or cell culture, although collaborative and past work includes fish models and a variety whole-animal mammalian systems.

Gokhan Mutlu
The University of Chicago

Gokhan Mutlu received his medical degree from Istanbul University Faculty of Medicine in 1992. He completed his residency in internal medicine and fellowship in Pulmonary and Critical Care Medicine at the University of Illinois at Chicago between 1994 and 2001. Mutlu worked as a faculty at Northwestern University between 2001 and 2014. He is currently Professor of Medicine and Chief of Section of Pulmonary and Critical Care Medicine at the University of Chicago. His research focuses on understanding the role of alveolar macrophages in acute lung injury and repair. As a part of this research focus, he studies the mechanisms by which particulate matter air pollution causes lung injury/inflammation and consequently acute thrombotic cardiovascular events. Specifically, he is interested in the role of catecholamines and adrenergic receptors in the pathogenesis of lung inflammation and vascular thrombosis. Mutlu has received funding from the American Heart Association, American Lung Association, and NIH to support his research. He has published more than 80 peer reviewed papers. He serves on the editorial board of PLoS One, AJP Lung and is an associate editor of the American Journal of Respiratory and Critical Care Medicine. He has received numerous awards for his work, including the ONES award from NIEHS in 2006. He is an elected member of the American Society of Clinical Investigation.

Timothy Nurkiewicz

West Virginia University School of Medicine

Timothy Nurkiewicz was funded by the NIEHS Outstanding New Environmental Scientist mechanism in 2007. In the past seven years, he has rose to the rank of associate professor (pending promotion to full professor this year). He is also the Associate Chair for Research in the Department of Physiology and Pharmacology at the West Virginia University School of Medicine in Morgantown, West Virginia. He currently leads the Xenobiotic Toxicology Initiative in the West Virginia University Center for Cardiovascular and Respiratory Sciences. He is a Past-President of the Allegheny-Erie Regional Chapter of the Society of Toxicology (SOT), as well as the Cardiovascular Toxicology Specialty Section (and a founding member). Nurkiewicz is the Director of West Virginia University's Inhalation Facility. He has been continuously funded by extramural agencies such as the National Institutes of Health, and Health Effects Institute since 2001. Nurkiewicz is a standing member of the Cardiac Biology/Regulation–Basic Sciences Study Section in the American Heart Association, and has served as an Ad Hoc member for NIH study sections. He currently serves on the editorial board of several toxicology journals. Nurkiewicz has been an adjunct scientist at the National Institute for Occupational Safety and Health since 2008.

Nurkiewicz's research program is active in the combined disciplines of microvascular physiology and toxicology, with a specific focus on pulmonary exposure to particulate matter and engineered nanomaterials. His laboratories use multiple animal models of inhalation exposure and subsequent *in vivo* (intravital microscopy) and *in vitro* (isolated microvessel) techniques. In 2004, the Nurkiewicz research program was the first to report that systemic endothelium-dependent dilation is impaired after pulmonary particulate matter exposure. In the past 10 years, they have been consistently revealing the mechanisms linking pulmonary toxicant exposure with systemic microvascular effects. Most recently, his research program initiated novel investigations in the field of maternal nanomaterial exposures and fetal microvascular ramifications.

Patricia Opresko

University of Pittsburgh Graduate School of Public Health

Patricia Opresko, Ph.D., is a tenured research associate professor in the Department of Environmental and Occupational Health at the University of Pittsburgh Graduate School of Public Health. She received her bachelors from the DeSales University in chemistry and biology and her doctorate from the Pennsylvania State University College of Medicine in biochemistry and molecular biology. She conducted a postdoctoral fellowship at the National Institute on Aging, investigating the molecular pathology of the premature aging disorder Werner syndrome. The research in Opresko's laboratory investigates the mechanisms of genomic and telomere instability associated with aging and aging related disease. Telomeres are protective DNA sequences at chromosome ends that profoundly influence life span, human disease and genome integrity. Her lab is studying genetic and environmental factors that shift the rates of telomere shortening in normal aging to accelerated rates that occur in premature aging syndromes and disease states. Currently she is studying the impact of environmental DNA damaging agents on telomere structure and function, and the roles of DNA repair enzymes in preserving telomeres. Opresko is well funded and published in the fields of DNA repair and telomere biology, and she has presented her work at numerous international conferences. She has published 43 articles in peer-reviewed scientific journals and 11 book chapters and reviews. Opresko has mentored several Ph.D. graduate students and post-doctoral fellows. She is a former recipient of the Ellison Medical Foundation New Scholars Award in Aging, and the Outstanding New Environmental Scientist Award sponsored by NIEHS. Her research is currently supported in part by several NIH sponsored awards: R01/NIEHS, R21/NIA, and SBIR/NIGMS grants. Opresko is a member of the American Association for Cancer Research and the Environmental Mutagenesis and Genomics Society. She currently sits on the Editorial Advisory Board Frontiers in Genetics of Aging, and is an associate editor for Mechanisms of Aging and Development.

Jill Poole

University of Nebraska Medical Center

Jill Poole, M.D. is an associate professor Division of Pulmonary, Critical Care, Sleep and Allergy Medicine and Medical Director of Allergy Services at the University of Nebraska Medical Center. She is a board-certified clinical allergist and immunologist with an active laboratory focused on understanding agriculture-related environmental organic dust-induced lung and systemic disease. This has been her focus for about nine years with grant funding from the National Institute of Environmental Health Sciences (prior K08 and ONES/ R01 grant currently) and the National Institute for Occupational Safety and Health. She has had several important findings as part of her funded work. She developed an animal model of organic dust-induced airway disease that resembles the chronic inflammatory adaptation response observed in humans. Next, she initiated a paradigm shift in this field by demonstrating a strong role for gram positive bacterial components as opposed to gram negative LPS with strong roles for TLR2 and MyD88 signaling pathways. Finally, she recently reported the first description of animal model connecting lung injury with bone loss consequences, and she is investigating the mechanisms underlying the lung-bone inflammatory axis crosstalk.

She enjoys collaborating with agriculture research centers in Nebraska and Colorado, particularly in human cross-sectional and epidemiological studies, and mentors Ph.D. and post-doctoral students, and pulmonary fellows. To highlight some of her services, she serves as a grant reviewer for NHLBI R13 study section, special issue editor for the International Immunopharmacology journal on asthma immunopathogenesis, invited in 2014 to serve on the editorial board for the Journal of Asthma, and chairs the occupational disease committee for the AAAAI. She has been invited to present her research discoveries at several allergy- and lung-focused meetings. In 2014, she presented a plenary talk at the American Academy of Allergy, Asthma and Immunology International meeting. She received tenure this year, and through her institution, she received the Basic Science Investigator 2011 Award Winner and Distinguished Scientist at UNMC. She has been the recipient of the 2011 American College of Allergy, Asthma and Immunology Young Faculty Research Award. She has been recognized as Best Doctor in America Award since 2009 as well as several local teaching awards.

Christina Porucznik

The University of Utah School of Medicine

Christina (Christy) Porucznik, Ph.D. MSPH, is an associate professor and the associate chief for research in the Division of Public Health of the Department of Family and Preventive Medicine. Her area of research interest is in appropriately timing measurement of exposures. In the environmental domain, she studies endocrine disruptors and reproductive endpoints, including fertility, pregnancy outcomes, and breastfeeding. Her other primary focus area is on prescription medications, primarily opioids, and the impact of policy changes on drug dispensing and adverse events.

Porucznik teaches in the Division of Public Health and serves on numerous graduate student committees (MPH, MSPH, and Ph.D.). She is the director of the Women in Medicine and Science program for the University of Utah School of Medicine and serves on the Academic Senate. Porucznik serves on the Board of Scientific Counselors for the National Center for Injury Prevention and Control of the Centers for Disease Control and Prevention (CDC). Before joining the faculty in 2005, Porucznik served as an Epidemic Intelligence Service Officer with the Centers for Disease Control and Prevention at the Utah Department of Health and as a Lieutenant Commander in the Commissioned Corps of the United States Public Health Service. She worked for the United States Environmental Protection Agency, Human Studies Branch, while completing graduate study in epidemiology at the School of Public Health at the University of North Carolina-Chapel Hill.

Jason Richardson
Rutgers Robert Wood Johnson Medical School

Jason Richardson, Ph.D., is a tenured associate professor in the Department of Environmental and Occupational Medicine at Rutgers Robert Wood Johnson Medical School and Resident Member of the Environmental and Occupational Health Sciences Institute. He also serves as deputy director of the NIEHS-funded T32 training grant at Rutgers University. He received his M.S. (1999) and Ph.D. (2002) degrees from Mississippi State University, where he conducted research on mixtures of organophosphate pesticides and the developmental neurotoxicity of organophosphates. He then completed postdoctoral training in molecular neuroscience at Emory University (2002-2005), where he focused on the role of pesticide exposure in Parkinson's disease. His research at EOHSI focuses on the role of environmental exposures and their interactions with genetic susceptibility contribute to neurological disease, which is funded by NIEHS, NINDS, and the Michael J Fox Foundation. Richardson has authored or co-authored more than 50 publications in the areas of developmental neurotoxicology, neurodegenerative disease, and pesticides. He received the Outstanding New Environmental Scientist Award from NIEHS and a Young Scientist Award from the American Society for Pharmacology and Experimental Therapeutics. Richardson is currently a member of the editorial boards of Toxicological Sciences, Neurotoxicology, Neurotoxicology and Teratology, Current Molecular Pharmacology, Toxics, and is an associate editor for BMC Neurology. He has served as a grant reviewer for several NIH panels, the Michael J. Fox Foundation, Health Canada, the UK MRC, Israel Science Foundation, and the United Kingdom Parkinson's Disease Society. He also served the SOT as Secretary/Treasurer of the Neurotoxicology Specialty Section for the past two years.

Joseph Shaw
Indiana University

Joseph Shaw, Ph.D., is an associate professor in the School of Public and Environmental Affairs at Indiana University and holds adjunct appointments in their School of Public Health and Center for Genomics and Bioinformatics. He is also a senior lecturer in the School of Biosciences at the University of Birmingham (20%), adjunct associate professor at the Mount Desert Island Biological Laboratory, and founding member of the Daphnia Genomics Consortium and Fundulus Genomics Consortium. Shaw earned his doctoral degree from the Center for Toxicology at the University of Kentucky in 2001. He then moved to Dartmouth College, where he received an NIEHS post-doctoral fellowship. His work at Dartmouth bridged studies of genes and their relationship to toxicologically relevant phenotypes with those that describe the effects environmental pollution on populations. He joined the faculty of the School of Public and Environmental Affairs at Indiana University, Bloomington in 2007 as an assistant professor. His current work at Indiana applies evolutionary theory, statistical analysis, and bioinformatics to investigate the interplay between the environment, mutation, genome structure, and phenotype in driving organism health and promoting adaptive outcomes in natural populations.

Angela Slitt
University of Rhode Island

Angela Slitt is an associate professor in the Department of Biomedical Sciences in the College of Pharmacy at the University of Rhode Island. Slitt received a B.S. with honors in molecular and cellular biology and a Ph.D. in pharmaceutical sciences from the University of Connecticut. Her graduate work focused on biochemical mechanisms of acetaminophen-induced liver and kidney injury. She was the recipient of an American Liver Foundation and Boehringer Ingelheim Predoctoral Fellowships. In 2000, Slitt joined the joined the laboratory of Curtis Klaassen at the University of Kansas Medical Center in the Department of Pharmacology, Toxicology, and Experimental Therapeutics as a NIH postdoctoral trainee and NRSA recipient. Her postdoctoral work focused on aspects of drug transporter expression in models of liver injury and microsomal enzyme induction. Her NIH NRSA postdoctoral fellowship examined induction of drug transporters and altered vectorial excretion of acetaminophen metabolites. After an extended maternity leave, Slitt joined the University of Rhode Island faculty in 2007. Her Transition into Independent Position award has addressed the role Nuclear Factor E2 Related-Factor 2 in cholesterol metabolism, biliary cholesterol excretion, and gallstone formation. Her NIH ONES award has been addressing how caloric restriction affects the Nrf2-Keap1 pathway, hepatic transport processes, and Bisphenol A excretion. ARRA funded supplements to Slitt's ONES award have allowed for successful summer research experiences, giving five high school, four undergraduate, and two high school teachers exposure to scientific research in academia. Other funded projects include studies of diabetes and obesity on drug transporter expression and evaluation of plant and food-derived polyphenolic compounds for anti-inflammatory activity. Along with research activities, Slitt is a URI Grand Challenges Teaching Fellow, teaching URI freshman about aspects of environmental health and is Pharmacology/Toxicology track coordinator. Dr. Slitt has more than 55 peer-reviewed publications, currently serves as an associate editor for BMC Pharmacology and Toxicology, and serves on the editorial boards of various journals, such as Toxicology and Applied Pharmacology and Journal of Biochemical and Molecular Toxicology.

Alexander Star
University of Pittsburgh

Alexander Star is an associate professor of chemistry and bioengineering at the University of Pittsburgh. His current research is focused on synthesis and properties of carbon nanomaterials and their applications in sensors, energy conversion devices, and nanomedicine. Originally from Kazakhstan, Professor Star received his B.Sc. and Ph.D. degrees in chemistry from Tel-Aviv University in 1994 and 2000, respectively. He then spent two years as a postdoctoral associate at California NanoSystems Institute at the University of California, Los Angeles, where he developed synthetic schemes to functionalize carbon nanotubes in a noncovalent fashion to improve their biocompatibility. Between 2002 and 2005, he served as senior scientist and manager of applications development at Nanomix, Inc. – a nanotechnology startup company – where he worked on development and commercialization of carbon nanotube-based sensors. He joined the chemistry faculty at the University of Pittsburgh in 2005. During his academic career, Star co-authored more than 85 peer-reviewed publications and was listed as a co-inventor on eight issued patents and more than 20 patent applications. His research was recognized by Intel Award, two University of Pittsburgh Innovator Awards, Chancellor's Distinguished Research Award, NSF CAREER Award, and NIEHS Outstanding New Environmental Scientist (ONES) Award.

Vishal Vaidya
Harvard Medical School

Vishal Vaidya, Ph.D., is an assistant professor of medicine and environmental Health at Harvard Medical School and Harvard School of Public Health and leads the Systems Toxicology Program in Therapeutic Sciences. He directs the Laboratory of Kidney Toxicology and Regeneration in the renal division of Brigham and Women's Hospital. His laboratory uses cellular systems, mouse models as well as human biospecimens, and applies methodologies at the interface of cell and molecular biology, systems pharmacology, and translational science in understanding kidney disease. Vishal has delivered more than 50 seminars as invited speaker and written more than 55 peer-reviewed publications, with more than 3,500 citations. His work supported by an NIH/NIEHS Pathway to Independence grant and, in collaboration with the Predictive Safety Testing Consortium, led to the first kidney toxicity biomarker (Kidney Injury Molecule-1) qualified by the US-FDA and the European Medicines Agency in 2008. In 2011, Vishal won the NIH/NIEHS Outstanding New Environmental Scientist (ONES) award.

The ONES-funded project not only led to the identification of urinary fibrinogen as a biomarker for early detection of kidney damage but also demonstrated the therapeutic potential of fibrinogen-derived $Bb_{15\text{-}42}$ peptide, which elicits 50 percent protection from kidney injury. In 2013, Vishal was selected as one of six North American scientists to win the Innovation in Regulatory Science Award from the Burroughs Wellcome Fund. In recognition of the seminal scientific contributions to the field of Toxicology, Vishal was awarded the Leading Edge in Basic Science Award at the annual Society of Toxicology (SOT) meeting, also in March 2014. Vishal directs the course "Understanding Biomarker Science: From Molecules to Images," offered through the Harvard Catalyst. The fifth iteration of this course (attended by more than 100 participants from academia, industry, the FDA, and NIH) was offered more than four days in March 2014.
Vishal also directs a five-credit course on Principles of Toxicology-Molecular and Translational Toxicology at HSPH in the Fall (EH504). Vishal acquired his Ph.D. degree from University of Louisiana in 2003 and completed his fellowship in nephrology from Brigham and Women's Hospital in 2007. He was awarded the Novartis Graduate Student Fellowship award from SOT and the National Kidney Foundation grant for his work during the graduate and postdoctoral training respectively.

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